REMARKS

Claims 1-32 and 48 are pending in this application. Claims 25 and 32 have been canceled, and new claims 49-56 have been added. Claim 1 has been amended to cancel proviso (a). Claims 2-9, 11-15, 17-19, 21, 24, 29-31, and 48 have been amended to add the phrase "or pharmaceutically acceptable salt thereof". Claim 23 was amended to replace the phrase "acceptable salts" with the phrase "acceptable salt thereof". Claim 26 has been further amended to independent format, as well to recite particular disorders. Claims 27 and 28 have been further amended to preserve antecedent basis. Claim 48 has been further amended to correct a minor typographical error. Support for the amendments can be found throughout the original specification and claims, for example, at pages 10, line 21 through page 11, line 34; and at page 12, lines 4-17 (deletion of proviso (a)). No new matter has been added. After entry of this amendment, claims 1-24, 26-31, and 48-56 will be pending in this application.

The specification has been amended merely to clarify the priority claim as set forth in the Application Data Sheet filed with the present application and in the official filing receipt mailed on October 9, 2007. No new matter has been added.

I. Supplemental Information Disclosure Statement

Applicants will be filing a supplemental information disclosure statement within the next few days for consideration by the Examiner. Applicants thank the Examiner for her consideration of the previously submitted information disclosure statement.

II. The Claims Are Enabled

Claims 25-26, and 29-31 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. In particular, the Office alleges that the "terms 'disorders of the central nervous system, cardiovascular disorders and gastrointestinal disorders" covers a broad array of different disorders that have different modes of action and different origins" (Office Action, page 2). The Office goes on to list several central nervous system disorders including AD, Parkinson's disease, Pick's disease, ALS, dementias, spinal

muscular atrophies, spinocerebellar degenerations, and Huntington's disease, stating that "the great majority of these have no treatment at all" (Office Action, pages 3-4). Citing to AD, the Office alleges that there is "clear evidence that the skill level in this art is low relative to the difficulty of the task" (Office Action, page 4). The Office concludes that "[w]here utility is unusual or difficult to treat or speculative, the examiner has authority to require evidence that tests relied upon are reasonably predictive of *in vivo* efficacy by those skill in the art" (Office Action, page 4).

As a preliminary matter, Applicants note that the Office appears to have acknowledged the enablement of the methods of treating **obesity** (claim 27) and **male erectile dysfunction** (claim 28), as these claims are not included in the listing of the rejected claims in section 1 of the Office Action (page 2). While Applicants disagree with the Office's conclusions regarding the enablement of the claimed methods, Applicants have canceled claim 25, solely to advance prosecution. Applicants have further amended claim 26 and added new claims 49-56. Applicants reserve the right to pursue the canceled subject matter in a future continuing application. Applicants respectfully assert that the methods of the amended and new claims are fully enabled for the reasons set forth below.

As will be recognized, the enablement requirement of § 112 is satisfied so long as a disclosure contains sufficient information that persons of skill in the art having the disclosure before them would be able to make and use the invention. *In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988) (the legal standard for enablement under §112 is whether one skilled in the art would be able to practice the invention without undue experimentation). In this respect, the following statement from *In re Marzocchi*, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971), is noteworthy:

> As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. Assuming that sufficient reason for such doubt does exist, a rejection for failure to teach how to make and/or use will be proper on that

> basis; such a rejection can be overcome by suitable proofs indicating that the teaching contained in the specification is truly enabling.
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> ... it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement.

Thus, any assertion by the Patent Office that an enabling disclosure is not commensurate in scope with the protection sought must be supported by evidence or reasoning substantiating the doubts so expressed. *In re Dinh-Nguyen*, 181 U.S.P.Q. 46 (C.C.P.A. 1974); *In re Bowen*, 181 U.S.P.Q. 48 (C.C.P.A. 1974). Further, the proper standard for an enablement inquiry rests on whether one skilled in the art would be able to make and use the invention without undue experimentation. *In re Wands*, 8 U.S.P.Q.2d at 1404. Factors for consideration in determining whether undue experimentation is necessary to make and use the invention include 1) the quantity of experimentation necessary; 2) the amount of direction or guidance presented; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims.

Applicants respectfully assert that the Office has failed to provide any reasoning or evidence for why a person of skill in the art would not accept that the claimed compounds would work to treat the specific disorders of claim 26 or to decrease food intake, induce satiety, and control weight gain. Further, Applicants respectfully assert that the art clearly demonstrates that one skilled in the art would accept that a 5-HT_{2c} agonist, such as compounds of the present application, would be useful in the claimed disorders for the reasons summarized below.

A. Methods of decreasing food intake, inducing satiety, and controlling weight gain (claims 29-31)

The Office rejects claims 29-31, reciting methods of decreasing food intake inducing satiety, and controlling weight gain but fails to give any reason for why these methods are not enabled. Indeed, in its discussion of the enablement rejection, the Office Action is completely

silent with regard to these particular methods. Hence, Applicants respectfully assert that the Office has failed to carry its burden under *In re Marzocchi* to provide evidence or reasoning to back up its assertions of non-enablement. Accordingly, the burden has not shifted to Applicants to provide rebuttal evidence to show the enablement of the claimed methods.

Nonetheless, Applicants respectfully note that the art clearly demonstrates that one skilled in the art would accept that compounds of the present application can decrease food intake, induce satiety, and control weight gain of a mammal without having to engage in undue experimentation. Compounds of the present application have been shown to be agonists of the 5-HT_{2c} receptor in an IP accumulation assay (see specification, Example 40, page 62, line 12, through page 63, line 5 (Table II). Further, 5-HT_{2c} agonists have been shown to increase satiety and induce undereating in animal studies, while 5-HT_{2c} knock-out mice have been shown to be hyperphagic and unresponsive to the anorectic effects of 5-HT_{2c} agonists (see e.g., Bickerdike, "5-HT_{2c} receptor agonists as potential drugs for the treatment of obesity", *Current Topics in Medicinal Chemistry*, 3:885-897 (2003), "Bickerdike"; and Tecott, et al., "Eating disorder and epilepsy in mice lacking 5-HT_{2c} serotonin receptors", *Nature*, 374:542-546 (1996)). Further, administration of mCPP, a 5-HT_{2c} agonist, to human obese subjects resulted in significant weight loss (Bickerdike, page 892). Hence, one skill in the art would accept that 5-HT_{2c} agonists, such as the compounds of claim 1, would be useful to decrease food intake, induce satiety, and control weight gain as recited by the claimed methods without engaging in undue experimentation. Accordingly, Applicants respectfully assert that the methods of claims 29-31 are fully enabled and request that the claim rejections be withdrawn.

B. Methods of treating depression, atypical depression, anxiety, obsessive-compulsive disorder, social phobia, panic states, sexual dysfunction, psychoses, schizophrenia, and epilepsy (amended claim 26 and new claims 49-55)

As noted above, Applicants have canceled claim 25 and amended claim 26 to recite particular disorders. The Office fails to provide any reason for why the particular treatment

methods of amended claim 26 are not enabled.[1] While the Office Action briefly mentions epilepsy in a laundry list of central nervous system disorders, the Office fails to give any specific reason for the alleged lack of enablement of this particular disorder. Further, in its discussion of the enablement rejection, the Office Action is completely silent to the remaining disorders in amended claim 26.[1] Hence, Applicants respectfully assert that the Office has failed to carry its burden under *In re Marzocchi* to provide evidence or reasoning to back up its assertions of non-enablement. Accordingly, the burden has not shifted to Applicants to provide rebuttal evidence to show the enablement of the claimed methods.

Nonetheless, Applicants respectfully note that the art clearly demonstrates that one skilled in the art would accept that a 5-HT_{2c} agonist can treat the disorders recited by amended claim 26, without having to engage in undue experimentation. *See e.g.,* Tecott, et al., "Eating Disorder and Epilepsy in Mice Lacking 5-HT_{2c} Serotonin Receptors", *Nature*, 374:542-546 (1996) (epilepsy-5-HT_{2c} knock-out mice subject to death from seizures); Isaac, "The 5-HT_{2C} receptor as a potential therapeutic target for the design of antiobesity and antiepileptic drugs" *Drugs of the Future* (2001), 26(4), 383-393 (epilepsy); Jenck, et al., "Antiaversive effects of HT_{2c} receptor agonists and fluoxetine in a model of panic-like anxiety in rats", *European Neuropsychopharmacology*, 8:161-168 (1998) (social phobias, panic disorders); Millan, et al., "HT_{2c} Receptors Mediate Penile Erections in Rats: Actions of Novel and Selective Agonists and Antagonists", *Eur. J. Pharmacol.* 325:9-12 (1997) (sexual dysfunction); Martin et al. "5-HT_{2C} receptor agonists pharmacological characteristics and therapeutic potential", *Journal of Pharmacology and Experimental Therapeutics* (1998), 286(2), 913-924 (sexual dysfunction-eliction of penile erections, obsessive-compulsive disorder-reduction in compulsive burying and schedule-inducted polydipsia in rats and compulsive scratching in squirrel monkeys); Bos et al., "Novel Agonists of $5HT_{2C}$ Receptors. Synthesis and Biological Evaluation of Substituted 2-{Indol-l-yl)-l-methylethylamines and 2-(Indeno[1,2-b]pyrrol-l-yl)-1-methylethylamines. Improved Therapeutics for Obsessive Compulsive Disorder, *Journal of Medicinal Chemistry* (1997), 40(17), 2762-2769 (obsessive-compulsive disorder-reduction in schedule-induced

[1] In section 2, the Office separately addresses the enablement of drug and alcohol addiction. Applicants address this portion of the rejection in section II.C of this response.

polydipsia in rats); Chahal, *ThomsonPharma, Literature and News Report*, May 17-18, 2000 (depression); Piesla et al., "Atypical Antipsychotic-like Effects of 5-HT_{2c} Agonists", *Abstracts of the 8th International Congress on Schizophrenia Research. British Columbia*, Canada, (April 28-May 2, 2001), Schizophrenia Research 49:95 (col. 2) (psychoses, schizophrenia); Clinical trial NCT00768612, "Study Evaluating Safety and Tolerability of Vabicaserin in Patients With Sudden Worsening of Schizophrenia Study", *http://clinicaltrials.gov/ct2/show/record /NCT00768612* (planned clinical trial for vabicaserin, 5-HT_{2C} agonist, for schizophrenia); and Rosenzweig-Lipson, et al., "Vabicaserin: effects of a novel 5HT2C agonist on medial prefrontal cortex neurotransmission, cognition and sensorimotor gating", *20th ECNP Congress*, Vienna, Austria (2007) (psychoses, schizophrenia). Accordingly, Applicants respectfully assert that the methods of claim 26 are fully enabled and request that the claim rejections be withdrawn.

C. Methods of treating drug and alcohol dependence (amended claim 26 and new claim 56)

Claims 25 and 26 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement with respect to "diagnosis, treatment, prevention, or alleviation...drug and alcohol addiction" (Office Action, page 5). The Office alleges that there "is not, and probably never will be a pharmacological treatment for 'drug addiction' generally" (Office Action, page 5). The Office asserts that alcohol and various drug addictions arise from involvement of different receptors and that, therefore, "[a]ll attempts to find a pharmaceutical to treat chemical addictions generally have thus failed" (Office Action, page 5).

Applicants respectfully assert that these conclusory statements do not carry the Office's burden to provide evidence or reasoning to back up its assertions of non-enablement as required by *In re Marzocchi*. The Office has cited no evidence of the supposed complete lack of treatments available for chemical addictions. Indeed, the record before the Office clearly shows that 5-HT_{2c} agonists have been shown to reduce cocaine, nicotine, and alcohol self-administration in animal studies (see e.g., Higgins, et al. "Serontonin and drug reward: focus on 5-HT_{2c} receptors", *European J. of Pharmacology*, (2003), 480:151-162, at page 155-156).

Accordingly, Applicants respectfully assert that methods of treating drug and alcohol addiction, such as those in claims 26 and 56 are fully enabled and request that the claim rejections be withdrawn.

III. Obviousness-Type Double Patenting

Claims 1, 2, 4-11, 13, 16, 17, 20, 24-27, 29-32, and 48 are rejected on the grounds of non-statutory obviousness-type double patenting over claims 1-6, 8-14, 17-22, 25, and 77 of U.S. Patent No. 6,953,787. Applicants will file a terminal disclaimer if appropriate upon an indication of allowable subject matter. Accordingly, Applicants respectfully request that the rejection be held in abeyance until the scope of the allowable subject matter becomes clear.

Claims 25-27 and 29-32 are provisionally rejected on the grounds of non-statutory obviousness-type double patenting over claims 1, 13-22, 31-47, 58-67, 73, and 75 of application serial no. 10/917,979. As the rejection is provisional in nature, Applicants will determine whether a terminal disclaimer is appropriate upon an indication of allowable subject matter.

Claims 1, 2, 4-11, 13, 16, 17, 20, 24-27, and 29-32 are provisionally rejected on the grounds of non-statutory obviousness-type double patenting over claims 1-3, 6-7, and 9-12 of application serial no. 11/599,050. As the rejection is provisional in nature, Applicants will determine whether a terminal disclaimer is appropriate upon an indication of allowable subject matter.

Claims 1, 2, 4-11, 13, 16, 17, 20, and 24-32 are provisionally rejected on the grounds of non-statutory obviousness-type double patenting over claims 47-50, 52-55, and 58-65 of application serial no. 11/560,953. As the rejection is provisional in nature, Applicants will determine whether a terminal disclaimer is appropriate upon an indication of allowable subject matter.

Claims 1, 2, 4-11, 13, 16, 17, 19-32, and 48 are provisionally rejected on the grounds of non-statutory obviousness-type double patenting over claims 1, 2, 4-11, 13, 16, 17, 19-32, and 48 of application serial no. 10/573,196. As the rejection is provisional in nature, Applicants will

determine whether a terminal disclaimer is appropriate upon an indication of allowable subject matter.

IV. Claim Objections

Claims 3, 12, 14, 15, and 18 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form. Upon an indication of allowable subject matter, Applicants will consider filing a terminal disclaimer to overcome the statutory obviousness-type double patenting rejections. Applicants respectfully request that the objections be held in abeyance until such time as the scope of allowable subject matter becomes clear.

V. Conclusion

Applicants respectfully request reconsideration of the rejections and objections of record and an indication of allowable subject matter. The Examiner is urged to contact Applicant's undersigned representative at (302) 778-8411 if there are any questions regarding the claimed invention.

The Commissioner is hereby authorized to debit any fee due or credit any overpayment to Deposit Account No. 06-1050. Further, if not accompanied by an independent petition, this paper constitutes a Petition for an Extension of Time for an amount of time sufficient to extend the deadline if necessary and authorizes the Commissioner to debit the petition fee and any other fees or credit any overpayment to Deposit Account No. 06-1050.

Respectfully submitted,

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